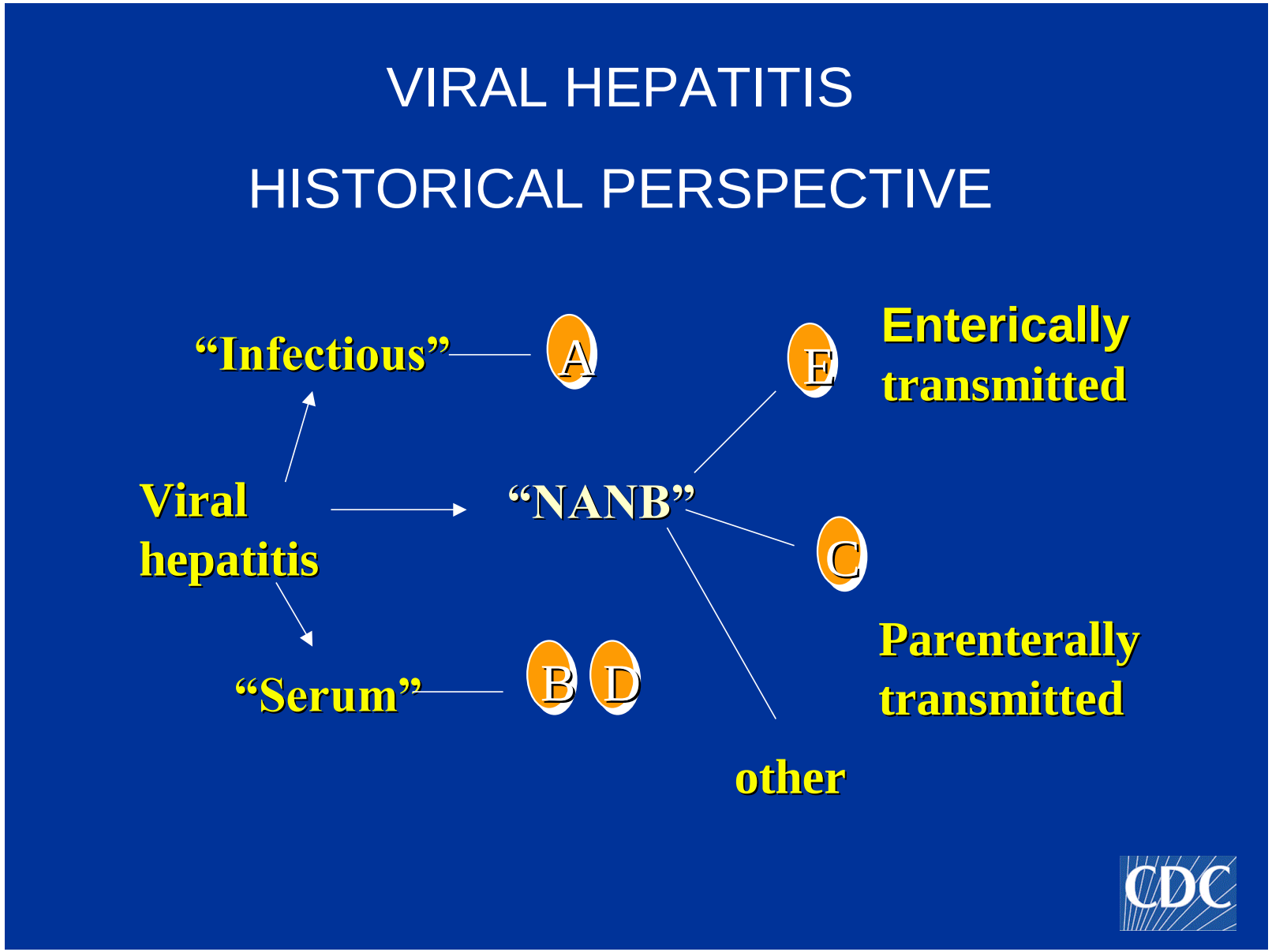
Hepatitis C, HCV/HIV Co-Infection, and HIV PREP

November 2015

History – Hep C discovered in 1989



HCV Background

- Epidemiology of chronic HCV infection in the United States
  - Prevalence
    - Approximately 3.2 million persons have chronic HCV infection
    - Infection is most prevalent among those born during 1945–1965
      - likely infected during the 1970s and 1980s
  - Incidence
    - CDC estimates > 20,000 cases per year
    - Persons newly infected with HCV are usually asymptomatic
      - under recognized and under reported
        - acute cases of hepatitis C **reported** only 1,229 to 1,778

HCV Background

- Risk factors for HCV infection
  - Current or former injection drug users
    - including those who injected "*only once many years ago*"
  - Blood/Organ Recipients
    - clotting factor concentrates before 1987
    - blood transfusions or solid organ transplants before July 1992
    - Now 1 in 2 million units transfused
  - Chronic hemodialysis patients
  - Health care workers after needlesticks
    - 1-10% if source HCV infected
  - Children born to HCV-positive mothers
  - Persons with HIV infection
  - Other
    - Intranasal drug use, non-sterile tattoos, other blood exposure

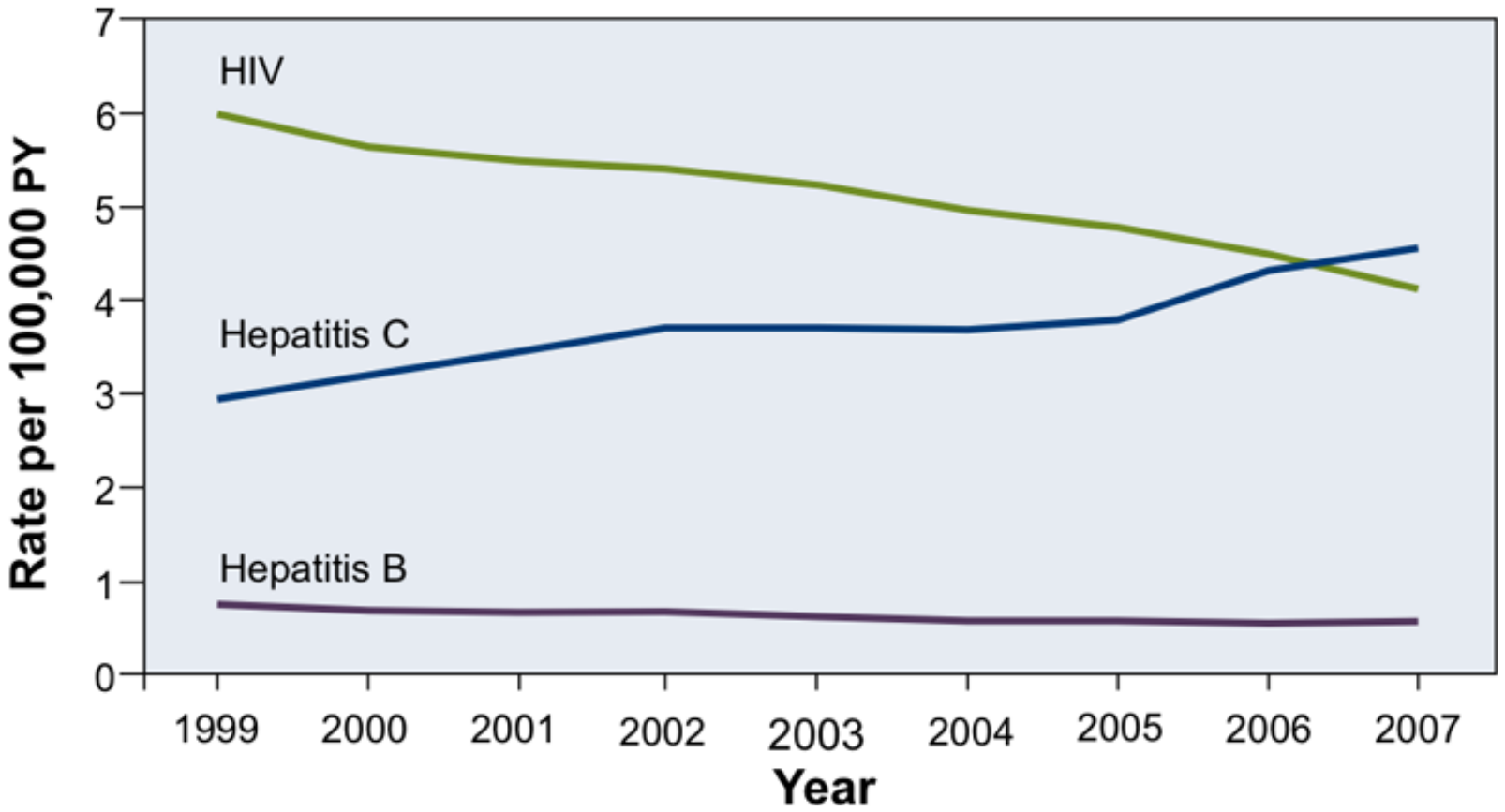
HCV Background

- Natural hx of HCV infection:
  - 20%–30% develop acute symptoms
    - symptoms resolve on own in about a month
  - 15%–25% of persons clear the virus from their bodies without treatment
    - do not develop chronic infection
    - reasons for this are not well known
    - can be re-infected
  - 75%–85% becomes chronic
    - often no symptoms for decades

HCV Background

- Natural hx of HCV infection
  - For every 100 persons infected with HCV:
    - 75–85 will go on to develop chronic infection
    - 60–70 will go on to develop chronic liver disease
    - 5–20 will go on to develop cirrhosis over a period of 20–30 years
    - 1–5 will die from the consequences of chronic infection (liver cancer or cirrhosis)
  - 15,106 deaths caused by HCV in 2007
  - Chronic HCV infection is the leading indication for liver transplants in the United States

HCV Background



*Mortality Rates = HBV, HCV, HIV listed as cause of death
Because of decedent can have multiple causes of death, a record listing more than 1 type of infection was counted for each type of infection

HCV Background

- HCV transmission
  - Most efficiently through large or repeated percutaneous exposures to infectious blood
    - Injection drug use
      - Young (aged 18–30 years) IDUs - 1/3rd are HCV-infected
      - Older IDUs (needle use in 1970's-80's) - approximately 70%–90%
  - Inefficient
    - Sex with an HCV-infected person
      - MSM > heterosexual
    - Sharing personal items contaminated with infectious blood
      - razors or toothbrushes

HCV Background

- Signs and symptoms
  - Acute HCV infection
    - Only occurs in 20%–30% of those newly infected with HCV
      - time period from exposure to symptom onset is 4–12 weeks
    - Non-specific
      - Fever, Fatigue, Abdominal pain, Loss of appetite, Nausea, Vomiting, Joint pain
    - Some Liver related
      - Dark urine, Clay-colored stool, Jaundice

HCV Background

- Signs and symptoms
  - Chronic HCV infection
    - Most are asymptomatic
      - fatigue
      - elevated liver enzymes detected during routine examinations
        - may have periodic returns to normal levels; can remain normal despite chronic liver disease
    - Chronic liver disease
    - Cirrhosis
      - Cytopenias, GI bleeding, ascites/swelling, encephalopathy
    - Liver cancer

HCV Background

- Testing – Who?
  - Persons born from 1945 through 1965 (screening)
  - Persons who have ever injected illegal drugs
  - Recipients of clotting factor concentrates made before 1987
  - Recipients of blood transfusions or solid organ transplants before 1992
  - Patients who have received long-term hemodialysis
  - Persons with known exposures to HCV
  - Patients with signs or symptoms of liver disease
  - Children born to HCV-positive mothers
  - All persons with HIV infection

HCV Background

- Testing – Who?
  - Routine HCV Testing is of "**uncertain need"**
    - Recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm)
    - Long-term steady sex partners of HCV-positive persons
    - Persons with a history of tattooing or body piercing
    - ***Intranasal cocaine and other non-injecting illegal drug users***
    - ***Persons with a history of multiple sex partners or sexually transmitted diseases***

HCV Background

- Testing – Who?
  - Routine HCV Testing Is **Not** Recommended
    - Health-care, emergency medical, and public safety workers
    - Pregnant women
    - Household (nonsexual) contacts of HCV-positive persons
    - General population

HCV Background

- Testing – How?
  - Screening tests
    - Test for antibody to HCV (anti-HCV)
    - Ab can be detected 4–10 weeks after infection
    - Detected in >97% of persons by 6 months
  - Confirmatory tests
    - Detect presence or absence of virus
    - HCV RNA polymerase chain reaction [PCR]
      - Often done quantitative to determine viral load
      - HCV RNA appears in blood and can be detected as early as 2–3 weeks after infection

HCV Background

- Management:
  - Education on:
    - Natural hx of disease
      - “decades, not days”
    - Transmission
      - Low but present risk for transmission to sex partners (1%/year)
      - Avoid sharing personal items (toothbrushes or razors)
      - Cuts and sores on the skin should be covered
      - Should not Donate blood, organs, tissue, or semen
      - **NOT** spread by sneezing, hugging, holding hands, coughing, sharing utensils or drinking glasses, or through food or water

HCV Background

- Management:
  - Evaluation for possible treatment:
    - ***NEW*** -- treatment recommended for ***all patients with chronic HCV infection***
      - except short life expectancies that cannot be remediated by treating HCV or transplantation
    - Abandon “triage approach”
      - degree of liver disease, extra-hepatic manifestations, risk of transmission
    - Other issues to consider:
      - Capacity to comply with treatment
      - Risk of re-infection
      - Medication interactions
      - Access to medication (insurance)

HCV Background

- Management:
  - Evaluation for possible treatment:

  - The risk of liver-related morbidity and mortality in an individual HCV-infected patient increases with the **severity of liver fibrosis**
    - Fibrosis stage (METAVIR system)
      - F0, no fibrosis
      - F1, portal fibrosis without septa
      - F2, portal fibrosis with few septa
      - **F3**, numerous septa without cirrhosis
      - **F4**, cirrhosis

    - *Recent* paradigm was to prioritize patients treatment based on stage of fibrosis
      - F0-F2 - wait for future therapies
      - F3/F4 - therapy should be offered
    - This approach *may still be enforced by insurers*
      - goes against current guidelines to treat everyone (barrier to care)

HCV Background

- Management:
  - Evaluation for possible treatment:

  - Modalities to evaluate for *severity* of chronic liver disease
    - Liver imaging
    - Biopsy
    - Special blood tests (Fibrosure)
    - Ultrasound based Elastography

  - Determination of HCV genotypes
    - needed to determine particular medications used for treatment
    - genotypes 1–6
      - genotype 1 is the most common in the United States

HCV Background

- Management:
  - Look for Co-infection (and vaccinate if applicable)
    - Hepatitis A and Hepatitis B
    - HIV testing
    - RPR testing
  - Look for other liver diseases
  - ***Advised to avoid alcohol***
    - accelerates cirrhosis
  - Consideration of *underlying risk factor (i.e. drug addiction)*
    - (this is what kills people most! – see next slide)

HCV Background

- May 2011 Journal of Hepatology, “Trends in mortality after diagnosis of hepatitis B or C infection: 1992–2006”
  - the authors looked at the ***cause of death*** in patients with Hepatitis C
    - They showed that the leading cause of death in the patients with Hepatitis C group was ***not*** **liver-related illnesses**.
    - 72% of deaths were the result of **drug overdose or suicide**

- Providing a patient’s with ready access and information about how to overcome addiction is vital

HCV Background

- Management:
  - Look for extrahepatic manifestation:
    - Chronic Hepatitis C issues outside the liver
      - endocrine, joints, skin, kidney, CNS, etc (fatigue)
      - Examples:
        - Diabetes mellitus
        - Glomerulonephritis
        - Essential mixed cryoglobulinemia and other vasculitis
        - Porphyria cutanea tarda
        - Non-Hodgkins lymphoma
        - Arthritis (may be rheumatoid like)

HCV Background

- Management:
  - Pregnancy and HCV Infection
    - Approximately 6 of every 100 infants born to HCV-infected mothers become infected with the virus
    - Transmission occurs at the time of birth
    - No prophylaxis is available to prevent it
    - No evidence that breastfeeding spreads HCV
    - Issues w/ HCV treatment and pregnancy
      - Ribavirin (teratogenicity)

HCV Background

- Treatment for chronic Hepatitis C
  - **Until recently** pegylated interferon and ribavirin, with possible addition of oral protease inhibitors
  - given for 24-48 weeks
  - treatment resulted in a “sustained virologic response” (SVR)
    - SVR = undetectable HCV RNA in the patient's blood 24 weeks after the end of treatment
      - Now checked 3 months after the end of treatment
    - SVR = Cure
    - SVR in 50%–90% of patients for traditional interferon based treatment
  - Treatment was very challenging to endure

HCV Background

HCV Background

- Treatment for chronic Hepatitis C
  - Now have “direct acting antiviral” drugs
    - treatment times of 8-24 weeks

- Sofosbuvir (Sovaldi™)
- Simeprevir (Olysio™)
- Ledipasvir and Sofosbuvir (Harvoni™)
- Ombitasvir, Paritaprevir, Ritonavir, Dasabuvir tablets (Viekira Pak™)
- Daclatasvir (Daklinza™)

HCV Background

- Treatment for chronic Hepatitis C
  - Direct acting antiviral drugs / interferon-free regimens
  - Tolerability / Safety / Convenience
    - Amazing improvement
  - Efficacy
    - SVR in high 90%'s for most clinical scenarios
  - Cost
    - Has dictated the current approach of triage
      - based on degree of liver disease, extra-hepatic manifestations, risk of transmission, etc.
  - See http://www.hcvguidelines.org/
    - website is constantly being updated given rapid evolution / changing treatment paradigms
      - Association for the Study of Liver Diseases (AASLD)
      - Infectious Diseases Society of America (IDSA)

HCV/HIV Co-infection

- Themes:
  - Co-infection is common
  - Increased transmission of HCV
    - HCV as an STI when co-infection present
    - Perinatal
  - Accelerated rates of liver damage (fibrosis)
  - Traditional poor response to HCV treatment
    - **Now optimism** w/ new direct acting antivirals
      - Still challenges

HCV/HIV Co-infection

- **EPIDEMIOLOGY**
  - Co-infection with HIV and HCV is common
  - share similar routes of transmission
  - In the United States, approximately 25-30 % of patients who are HIV-infected are also co-infected with HCV

  - Rates differ according to risk factor:
    - Example: HCV seroprevalence in HIV-infected in *intravenous drug users* was 73 percent in one large study

HCV/HIV Co-infection

- **EPIDEMIOLOGY**
- The *sequence* of infections is often different based on *risk factors*:
  - injection drug users usually acquire HCV before HIV infection
  - men who have sex with men (MSM) typically are infected with HIV before they acquire HCV infection

HCV/HIV Co-infection

- **In Men who have sex with men**
  - HIV-infection associated with a **six-fold** increase in HCV incidence
  - Seroprevalence of HCV in HIV-infected MSM is **increasing**
    - especially in those whose predominant risk factor is unsafe sex
  - HCV is **sexually transmitted** more commonly among HIV-infected MSM
    - MSM with HIV infection have higher seminal fluid HCV values than HIV-uninfected MSM
      - more likely to transmit HCV
    - HCV is **not** as common among HIV-uninfected MSM

HCV/HIV Co-infection

- **Perinatal transmission**
  - Vertical transmission of HCV appears to be facilitated by HIV co-infection
  - maternal co-infection increases the odds of vertical HCV transmission by approximately 90 percent compared with maternal HCV infection alone
    - 10.8 versus 5.8 percent in large study published in CID 2014
  - HCV has been isolated from cervicovaginal fluid in HIV-seropositive women, but not in women with HCV alone
    - may explain the higher rates of perinatal HCV transmission observed in the setting of coinfection

HCV/HIV Co-infection

- Virology
  - Both RNA viruses
    - HIV (a retrovirus)
    - HCV (a flavivirus)
  - viral production rates
    - HIV 10(10) virions a day
    - HCV 10(12) virions a day
  - During the chronic stage of either HIV or HCV infection, a relatively stable viral load or "set point" is maintained
    - Usually in the “thousands” for HIV & in the “millions” for HCV

HCV/HIV Co-infection

- Virology
  - HCV RNA levels increase after HIV seroconversion
    - may be related to immunosuppression
    - the envelope protein of HIV (gp120) also increases HCV replication
  - HCV viremia is inversely correlated with lower CD4 counts
  - Higher HCV mutational rates
    - increased sequence variability of the HCV genome has been noted in HIV/HCV-coinfected individuals
    - harder on the host immune system to mount effective response

HCV/HIV Co-infection

- Pathogenesis
  - HIV/HCV co-infected patients have accelerated rates of fibrosis progression compared with patients with HCV alone
    - decreased immune response to HCV antigens in HIV-infected patients
  - HIV-associated non-directed immune activation
    - increased pro-inflammatory cytokines
    - activated hepatic cells increase collagen formation (fibrosis)

HCV/HIV Co-infection

- **Effect of HIV on the Natural History of HCV**
  - Higher rates of morbidity and mortality related to liver disease
    - mortality rate, 59 versus 39 per 1000 person-years (co-infected vs mono-infected)
  - Less likely to clear HVC viral infection
    - Less than 10% clear (>90 % become chronic)
  - More rapid rates of liver fibrosis
    - Paired biopsy studies
      - 2.5 years between biopsies, progression of at least one fibrosis stage was observed in 34 percent, and progression of two or more stages was observed in 9 percent
      - rapid progression to cirrhosis has also been reported
  - Higher risk of hepatic decompensation compared with HCV mono-infected patients
  - Hepatocellular carcinoma (HCC) occurs faster and is associated with shorter survival in HIV/HCV co-infected patients
    - Co-infected patients (after 26 years)
    - HCV mono-infected patients (after 34 years)

HCV/HIV Co-infection

- Testing for HCV with HIV co-infection
  - Sensitivity and specificity of third generation HCV Ab ELISA assays approach 99 percent
  - However, patients with severe immunosuppression (CD4 cell counts **<100 cells/mm3**) *may have a false negative serology*
    - due to impaired antibody formation
    - occurs in than less than 5 percent of patients
  - In HIV-infected patient w/ low CD4 consider hepatitis C RNA testing
    - esp. if has significant risk factors for HCV

HCV/HIV Co-infection

- Effect of ART on HCV progression
  - Many studies suggest that ART is beneficial
  - Demonstrated benefits:
    - Decline in liver-related mortality
    - Slower rates of fibrosis progression
    - Lower risk of end-stage liver disease
      - Almost percent lower likelihood of hepatic decompensation
    - Lower rates of hepatocellular carcinoma

HCV/HIV Co-infection

- HCV and Hepatotoxicity with ART
  - HCV increases the risk of hepatotoxicity from antiretroviral therapy
    - Some ART regimens are more hepatotoxic than others
      - Ex. nevirapine, ritonavir
    - ART-associated hepatotoxicity may be related to immune reconstitution
      - hepatotoxicity often correlates with a rise in CD4 count
  - Benefit of antiretroviral therapy outweighs the risk of liver injury
    - close laboratory follow-up is prudent

HCV/HIV Co-infection

- Treating HCV in setting of HIV co-infection
  - Interferon based regimens (old news)
    - HIV/HCV co-infected patients traditionally had lower response rates to HCV treatment
    - With peginterferon and ribavirin
      - overall SVR rates 14 - 35 percent compared with 42 - 46 percent in mono-infected patients
  - Direct Acting antivirals (now):
    - HIV/HCV co-infected patients appear to have comparable SVR rates to mono-infected patients w HCV
      - > 90%
      - **curative all-oral treatment is a possibility for most patients w/ HIV-infection!**
    - Major issue at this point is potential drug-drug interactions w/ ART and HCV meds
      - should take into account w/ ART regimen selection

HCV/HIV Co-infection

- Treating HCV in setting of HIV co-infection
  - Due to cost concerns of HCV treatments, prioritizing patients who may benefit most from HCV antiviral treatment has been advised (but this approach should be abandoned)
    - Factors:
      - HCV genotype
      - History of prior HCV treatment
      - Stage of underlying liver fibrosis
      - Potential drug interactions between ART and HCV antiviral agents

HCV/HIV Co-infection

- Effect of HCV on the *natural hx of HIV*
  - Various studies that suggest:
    - HCV seropositivity is an independent risk factor for progression to *AIDS and death*
      - AIDS-defining events when HCV-seropositive
        - relative risk 2.6 of
      - Increased mortality
        - standardized mortality rate HCV co-infection vs HCV-negative 20.8 compared with 4.8
    - *Lower rate of CD4 cell gains* among patients who had chronic HCV infection
    - Greater rates of *non-hepatic complications*
      - osteoporosis / bone fractures
      - chronic kidney disease
      - possibly additional cardiovascular risk
  - The factors responsible are not well understood
    - may result from generalized immune activation

HIV Control

Strategies to Control HIV

- Behavior modification
  - safer sex campaigns / education
  - condoms
- Case finding / HIV testing
- Blood supply testing
- Injecting drug users
- Circumcision
- Medical therapies
  - HAART
    - effect on transmission
    - pre-exposure prophylaxis
    - post-exposure prophylaxis
    - prevention of mother to child transmission
  - Microbicides
  - Treatment of co-infections and STD's
  - HIV vaccines

HIV Control: Medical Therapies

- Pre-Exposure Prophylaxis (PrEP)
  - Using ARVs daily or as needed on HIV ***uninfected*** individuals to prevent HIV transmission
  - Basis:
    - single dose nevirapine to HIV-infected women during labor and to their newborns
      - reduced transmission of HIV by about 50 percent
    - Animal studies
  - Concerns:
    - only partially effective
    - antiviral resistance
    - slippery slope thinkers – increased risky behavior

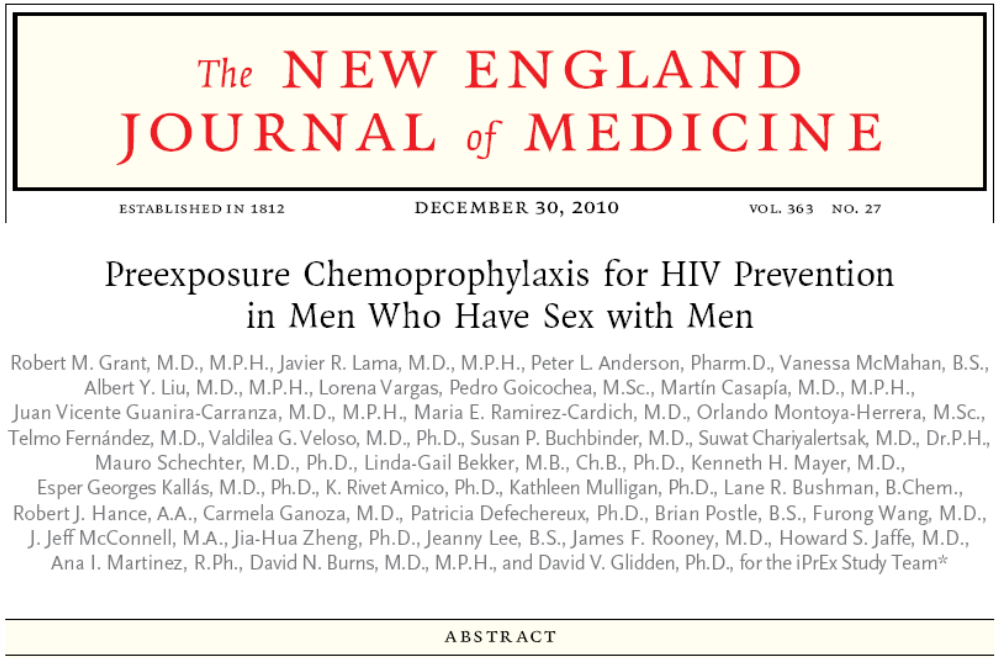
HIV Control: Medical Therapies

Table 1 ONGOING AND PLANNED PrEP TRIALS AS OF APRIL 2008

Location	Sponsor/ Funder	Population (mode of exposure)	Intervention Arms	PrEP strategy(ies) being tested	Status/Expected completion
United States	CDC	400 men who have sex with men (penile/rectal)	1	Tenofovir disoproxil fumarate (TDF)	Fully enrolled – Ongoing 2009
Thailand	CDC	2,400 injecting drug users (parenteral)	1	TDF	Enrolling / 2009
Botswana	CDC	1,200 heterosexual men and women (penile and vaginal)	1	TDF+emtricitabine (FTC) (switched from TDF Q1 2007)	Enrolling / 2010
Peru, Ecuador, US, additional sites TBD (iPrEX Study)	NIH, BMGF	3,000 men who have sex with men (penile/rectal)	1	TDF+FTC	Enrolling / 2010
Kenya, Uganda (Partners Study)	BMGF	3,900 serodiscordant couples (penile and vaginal)	2	TDF; TDF + FTC	Planning / 2012 Anticipated start Q2/2008
Kenya, Malawi, South Africa, Tanzania (FEMPrEP)	FHI, USAID	3,900 high-risk women (vaginal)	1	TDF+FTC	Planning / 2011 Anticipated start Q3/2008
Malawi, South Africa, Zambia, Zimbabwe (VOICE Study)	MTN, NIH	4,200 sexually active women (vaginal)	3	TDF; TDF+FTC; TDF gel	Planning / 2011 Anticipated start Q4/2008

BMGF – Bill & Melinda Gates Foundation; CDC - US Centers for Disease Control; FHI – Family Health International; MTN – Microbicide Trials Network; NIH – US National Institutes of Health; USAID – United States Agency for International Development

HIV Control: Medical Therapies



The NEW ENGLAND JOURNAL of MEDICINE

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Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

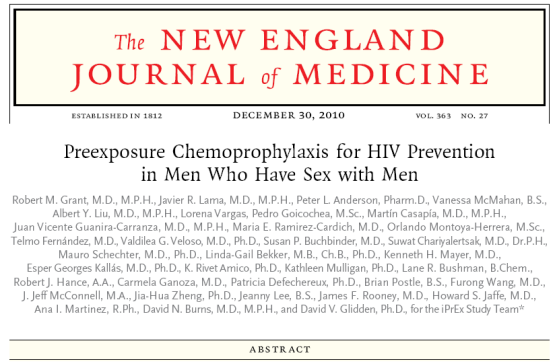
Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

ABSTRACT

- 2499 HIV (-) MSM
- 100 became infected during follow-up (median, 1.2 years)
  - 36 in the pre-exposure prophylaxis group
  - 64 in the placebo group
- 44% reduction in the incidence of HIV

HIV Control: Medical Therapies

- results continued …
  - Does PrEP increase risk behavior?
    - Condom use increased
    - No differences between the treatment / placebo arms in:
      - number of STDs
      - high-risk sexual practices
    - Adherence required
      - drug levels correlated with a protective effect
      - drug was detected in only 9% of participants w/ newly acquired HIV infection vs 51% of participants who did not acquire HIV
      - Sub-study of the trial:
        - protective efficacy of tenofovir-emtricitabine increased to **≥96 %** for those whose drug levels suggested that they **took at least four doses per week**



HIV Control: Medical Therapies

- More of PrEP
  - N Engl J Med. 2012 Jul 11
    - Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women.
      - conducted in heterosexual serodiscordant couples
      - reduced the risk of acquiring HIV infection by 75%
  - The Lancet 2013 June 15
    - Antiretroviral prophylaxis for HIV infection in injecting drug users
  - PROUD study (England)
    - Presented at Conference on Retroviruses and Opportunistic Infections (CROI 2015)
    - effectiveness was 86%
  - Clinical Infectious Diseases; September 2015
    - "No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting"
  - Overall take: 50-100% protection

HIV Control: Medical Therapies

- July 16 2012 FDA approval of Emtricitabine/tenofovir for PrEP
  - daily oral antiretroviral drug to reduce the risk of sexual acquisition of HIV

  - Issues:
    - Will it increase risk behavior?
    - Resistance?
    - Toxicity long term?
    - Who to treat?
    - Who pays?

HIV Control: Medical Therapies

- Acquired drug resistance during PrEP:
  - emtricitabine
    - the genetic barrier to resistance is low
    - M184V
  - tenofovir
    - the genetic barrier to resistance is high
    - K65R; uncommonly seen in clinical practice

- In the PrEP trials, most cases of drug resistance have occurred in patients who were retrospectively found to have acute HIV infection at enrollment

HIV Control: Medical Therapies

- Adverse event to PrEP:
  - Generally well tolerated in studies to date
  - Renal
    - Limit to patients w/ normal renal function
      - in the NEJM published iPrEX trial 10 creatinine elevations led to discontinuation of a study drug
      - all but one elevation resolved with treatment discontinuation
  - Bone
    - subclinical bone demineralization
    - no differences in the rate of fracture occurrences
  - Caution in Hep B co-infected
    - May induce a flare if adherence an issue

HIV Control: Medical Therapies

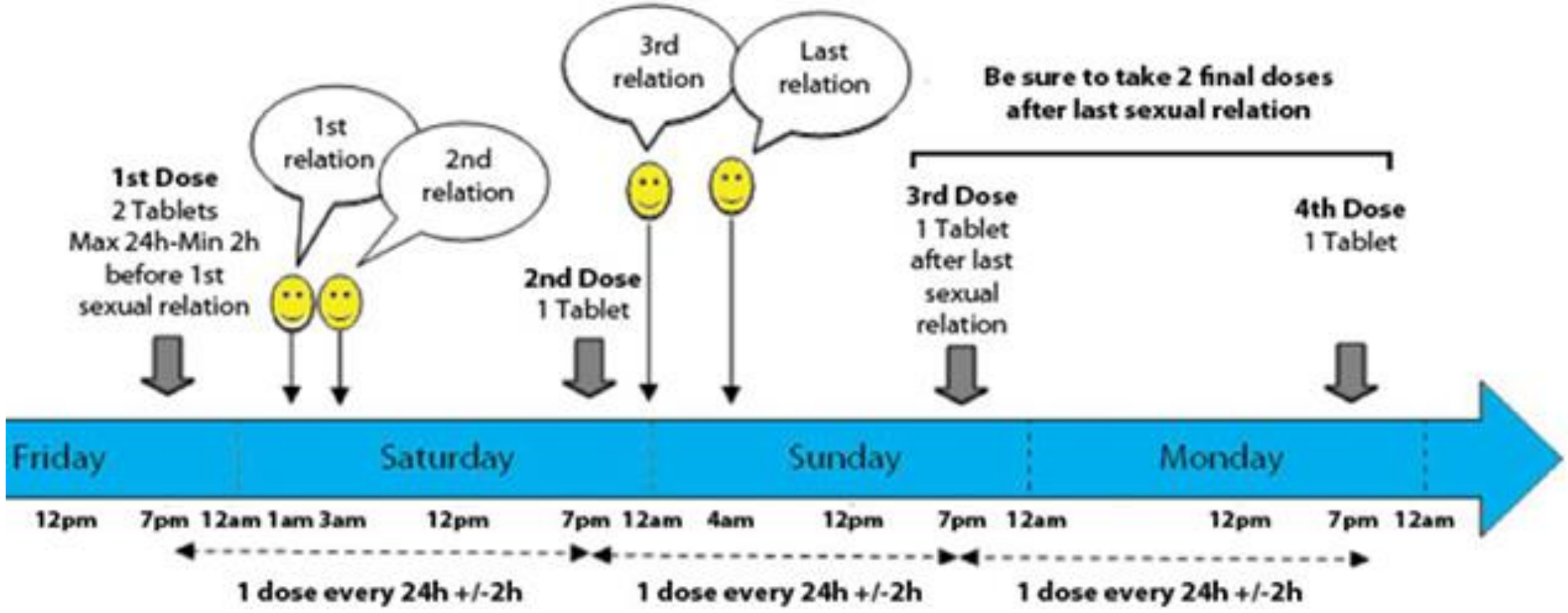
- Who should get PrEP?
  - HIV-uninfected sexual partners of an HIV-infected individual (sero-discordant partner)
    - likely not needed if HIV-infected partner has confirmed suppressed HIV RNA
  - MSM who have reported high-risk sexual behaviors in the past 6 months
    - ***or had a documented sexually transmitted infection***
  - Heterosexual men / women who infrequently use condoms and have sex with partners who are at high risk of HIV-infection
    - injection drug users, MSM, partners from areas where there is a high HIV prevalence
  - Individuals who have used post-exposure prophylaxis more than twice in the past year
  - Injection drug users who, in the last six months, report sharing needles/equipment

HIV Control: Medical Therapies

- Cost of PrEP
  - estimated cost of **daily** emtricitabine-tenofovir is $1425 monthly

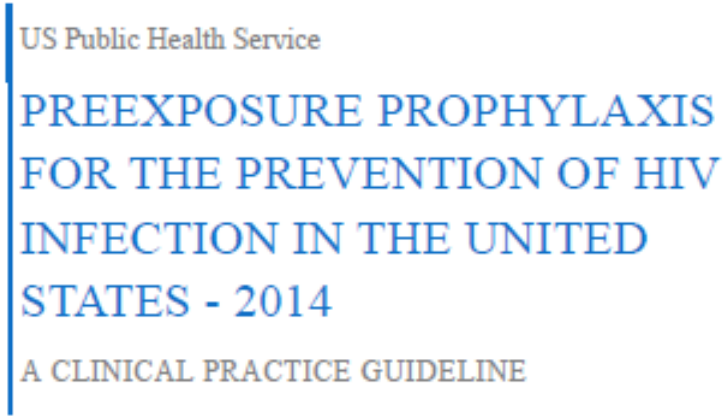
  - Ann Intern Med. 2012;156(8):541.
  - “The cost-effectiveness of pre-exposure prophylaxis for HIV prevention in the United States in men who have sex with men”
    - PrEP was evaluated in both the general MSM population and in high-risk MSM (average of 5 partners per year)
    - use in high-risk MSM compares favorably with other interventions that are considered cost-effective
    - would result in annual PrEP expenditures of more than $4 billion

“On-Demand” PrEP – 86% effective (IPERGAY trial)



HIV Control: Medical Therapies

- “Time for debate on the effectiveness of PrEP is over”
    - DAN GROOVER JANUARY 4, 2015
- Under-utilized:
    - Currently only a few thousand individuals are using PrEP nationwide
    - CDC says that at least 500,000 people could benefit from using it
    - August 2014 study by the Kaiser Family Foundation found that 80% of gay and bisexual men knew “only a little” or “nothing at all” about PrEP


US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE

HIV Control

Strategies to Control HIV

- Behavior modification
  - safer sex campaigns / education
  - condoms
- Case finding / HIV testing
- Blood supply testing
- Injecting drug users
- Circumcision
- Medical therapies
  - HAART
    - effect on transmission
    - pre-exposure prophylaxis
    - post-exposure prophylaxis
    - prevention of mother to child transmission
  - Microbicides
  - Treatment of co-infections and STD's
  - HIV vaccines

HIV Control: Medical Therapies

- “Microbicide"
  - topical agent that can be applied vaginally
  - Locally applied “PrEP”
  - Vaginal chemoprophylaxis
  - female-controlled method of prevention

  - Various mechanisms:
    - physical barrier
    - non-selective inactivation of the virus
    - specific antiviral activity

HIV Control: Medical Therapies

- Microbicides
  - Currently available spermicides do not protect against transmission of HIV
    - nonoxynol 9 might increase the risk for HIV sexual transmission
      - irritative effects on the vaginal epithelium
  - Others:
    - P3 cellulose sulfate gel halted 2007
      - increased risk of HIV
    - Carraguard microbicide trial 2008
      - showed safety, but no efficacy

HIV Control: Medical Therapies

- Finally success
  - July, 2010 XVII International AIDS Conference
    - Tenofovir Vaginal Gel
      - First Microbicide to Prevent HIV Infections
      - Application of gel or placebo before & after sex
        - high prevalence area (pregnant women 21.0-51.1% HIV positive)
      - 889 sexually active HIV (-) women
        - 38 women in the tenofovir group became HIV-positive
        - 60 women in the placebo group became HIV-positive
      - 39% lower risk of HIV overall
        - 54% reduction if used routinely / correctly
    - Ongoing studies w/ topically applied anti-retrovirals
      - Both intravaginal and enema deliver methods
        - Ex. vaginal ring

- QUESTIONS / COMMENTS?